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In vitro and in vivo activity of a novel series of radical trapping agents in model systems of CNS oxidative damage.

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Many laboratory and clinical studies suggest that oxygen radical formation and resultant cell damage contribute to CNS injury following stroke and neurotrauma. Accordingly, antioxidants represent a viable therapeutic approach for management of CNS oxidative damage. Recently, several investigators have reported that the spin trap PBN protects against stroked-induced damage and reduces aging-associated neurological deficits. We have prepared and tested a cyclic analog of PBN, MDL 101,002, in a number of in vitro and in vivo assays designed to assess its neuroprotective properties. MDL 101,002 was found to be an effective .OH trap, to inhibit lipid peroxidation, and to decrease infarct size in a gerbil model of stroke. These results further indicate that oxidative damage arising from stroke contributes to infarct formation, and that spin traps are effective in ameliorating ischemia and reperfusion-induced CNS injury.

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